

**REMARKS**

Entry of the foregoing amendments is respectfully requested.

**Summary of Amendments**

Upon entry of the foregoing amendments, claims 15 and 35 are amended, whereby claims 15-20 and 22-35 will remain pending, with claims 15, 26 and 34 being independent claims.

The amendments to claim 15 and 35 consist merely in the deletion of the term “about”

Applicants emphasize that the amendments to claims 15 and 35 are without prejudice or disclaimer, and Applicants expressly reserve the right to prosecute these claims in their original, unamended form in one or more continuation and/or divisional applications.

Applicants further point out that entry of the present amendments is proper because they do not raise any new issues and do not require any further search.

**Summary of Office Action**

As an initial matter, Applicants note with appreciation that the Examiner has withdrawn the rejection of claims 15-20 under 35 U.S.C. § 102(b) as allegedly being anticipated by Takeuchi et al., U.S. Patent No. 5,624,962 (hereafter “TAKEUCHI”), and the rejection of claims 15-20 under 35 U.S.C. § 102(b) as allegedly being anticipated by Thut et al., U.S. Patent No. 5,505,922 (hereafter “THUT”).

Claims 15-20 (claim 21 is cancelled) stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Busciglio, U.S. Patent No. 4,748,022 (hereafter “BUSCIGLIO”).

Claims 15-20 and 22-34 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over THUT.

Claims 15-20 are newly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over TAKEUCHI.

**Response to Office Action**

Reconsideration and withdrawal of the rejections of record are respectfully requested, in view of the foregoing amendments and the following remarks.

***Response to Rejection of Claims under 35 U.S.C. § 102(b) over BUSCIGLIO***

Claims 15-20 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by BUSCIGLIO. In this regard, the Examiner appears to take the position that a pH of about 3.0 to 7.5 as recited in present claim 15 can be considered to encompass a pH of 8 as disclosed by BUSCIGLIO. Moreover, the Examiner also appears to take the position that in view of the allegedly small difference between a pH of about 7.5 and the pH of 8 recited in BUSCIGLIO, the term “about” renders claim 15 indefinite.

Applicants respectfully disagree with the Examiner in this regard. Nevertheless, merely in order to advance the prosecution of the present application Applicants have deleted the term “about” from independent claim 15, thereby rendering this rejection moot.

***Response to Rejection of Claims under 35 U.S.C. § 103(a) over THUT***

Claims 15-20 and 22-34 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over THUT. In this regard, the rejection essentially alleges that THUT mentions “mixtures” of anesthetics and asserts that “the term “mixtures” is generally understood to be 1 : 1”. The rejection further essentially alleges that one of ordinary skill in the art would recognize that the weight ratio of two anesthetics is a result-effective variable and would thus optimize the weight ratio as a matter of routine experimentation.

Applicants respectfully traverse this rejection. Specifically, it is pointed out that the Examiner has not provided any written (or other) support for the allegation that “the term “mixtures” is generally understood to be 1 : 1”.

Applicants also emphasize again that one of ordinary skill in the art will understand that the statement in THUT that the various types of local anesthetics mentioned therein “can be present in the anesthetic pharmaceutical combination alone or as a mixture of two or more thereof” is not more than a mere boilerplate statement which neither teaches or suggests that using a combination of an amide-type local anesthetic and an antihistamine-like anesthetic is associated with any advantage.

Applicants respectfully submit that the Examiner’s corresponding counterargument, i.e., that benadryl is the only antihistamine anesthetic mentioned in THUT, wherefore one of ordinary skill in the art allegedly would mix benadryl with any of the other anesthetics mentioned in THUT is based on hindsight. Moreover, benadryl is not even mentioned among the group of apparently preferred anesthetics as mentioned in claims 3 and 11 of THUT, all of which are amide-type anesthetics. Further, claims 3 and

11 recite “mixtures of two or more” of these amide-type anesthetics, which suggests that “the mixture of two or more thereof” referred to in col. 3, line 49 of THUT refers to mixtures of anesthetics of the same type (in particular, amide-type).

It further is noted that regarding the osmotic pressure ratio recited in, e.g., independent claim 26 and Applicants’ argument that one of ordinary skill in the art would not consider the osmotic pressure ratio to be a result effective variable which needs to be optimized the rejection essentially alleges that from HARAGUCHI et al., U.S. Patent No. 6,008,256, col. 6, lines 28-44 in combination with NISHIBE et al., US 2003/0008019, paragraph 11 it is known that the osmotic pressure ratio controls absorption of a drug.

In this regard, it is pointed out that from paragraph 11 of NISHIBE et al. it even becomes clear there is no established and predictable relationship between the osmotic pressure ratio of a drug and its absorption. For example, according to paragraph [0011] of NISHIBE et al. “absorption through the rat nasal mucosa of growth hormone releasing factor is higher when the preparation has an osmotic pressure ratio of 1 (osmotic pressure of 290 mOsm) or lower, and … it is higher when secretin has an osmotic pressure ratio of 1 (osmotic pressure of 290 mOsm) or greater”. Accordingly, the Examiner has also failed to provide support for the allegation that it is known that the osmotic pressure ratio controls absorption of a drug.

Applicants submit that for at least all of the foregoing reasons and the additional reasons set forth in the response to the previous Office Action, THUT is unable to render obvious the subject matter of any of the claims submitted herewith, wherefore the rejection of claims 15-20 and 21-34 under 35 U.S.C. § 103(a) over THUT is without merit and withdrawal thereof is again respectfully requested.

***Response to Rejection of Claims under 35 U.S.C. § 103(a) over TAKEUCHI***

Claims 15-20 are newly rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over TAKEUCHI. The rejection essentially asserts that TAKEUCHI mentions “mixtures” of anesthetics and alleges again that “the term “mixtures” is generally understood to be 1 : 1”. The rejection further essentially alleges that one of ordinary skill in the art would recognize that the weight ratio of two anesthetics is a result-effective variable and would thus optimize the weight ratio as a matter of routine experimentation.

This rejection is respectfully traversed as well. Applicants point out again that the Examiner has not provided any evidence whatsoever which would support the allegation that “the term “mixtures” is generally understood to be 1 : 1”. Neither has the Examiner provided any written or other evidence which would support the allegation that one of ordinary skill in the art would recognize that the weight ratio of two anesthetics is a result-effective variable

It further is pointed out that the compositions of TAKEUCHI have the property of thermosetting gelation at body temperature. The Examiner has failed to explain why one of ordinary skill and would be motivated or have an apparent reason to use a composition which forms a gel at the body temperature of a mammal (see, e.g., col. 3, line 53 of TAKEUCHI) for injection in oral surgery or dental treatment. Neither has the Examiner provided an example of any composition which forms (or is) a gel at body temperature and has been used (and is save) for injection.

TAKEUCHI clearly does not support an assumption that it is possible, let alone save, to use the compositions disclosed therein for injection. Specifically, in col. 1, lines

6-17 TAKEUCHI merely indicates that the aqueous drug composition taught therein is a "fluid liquid at room temperature or lower and, when administered to eyes or body cavities or spread on skin, gelation happens at body temperature of mammal, so as to achieve a greater degree of bioavailability of the pharmacologically effective component and maintain the effect of the drugs for long period". The body cavities mentioned in col. 4, lines 39-41 of TAKEUCHI are rectum, urethra, nasal cavity, vagina, auditory meatus, oral cavity and pouch.

Applicants submit that for at least all of the foregoing reasons, TAKEUCHI fails to render obvious the subject matter of any of the present claims, wherefore the rejection of claims 15-20 under 35 U.S.C. § 103(a) over TAKEUCHI is without merit and withdrawal thereof is warranted.

### **CONCLUSION**

In view of the foregoing, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. If any issues yet remain which can be resolved by a telephone conference, the Examiner is respectfully invited to contact the undersigned at the telephone number below.

Respectfully submitted,  
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